

1/3/02

What is claimed is:
Claims:

1. An isolated polypeptide which possesses PI3-kinase activity when produced by recombinant production in insect cells.
2. A polypeptide derivative of a polypeptide as defined in claim 1 and which has PI3-kinase activity and binds, when associated with a p85 mammalian PI3-kinase subunit, to a phosphopeptide which includes the YXXM motif, the tyrosine being phosphorylated.
3. A polypeptide as claimed in claim 1 or claim 2 and which is capable of association with p85 subunits of mammalian PI3-kinases to produce active complexes.
4. A polypeptide having the amino acid sequence of Figure 9, or exhibiting significant sequence homology with the amino acid sequence of Figure 9 and possessing PI3-kinase activity.
5. A polypeptide as claimed in any one of the preceding claims and which is of human origin.
6. An antibody to a polypeptide as defined in any one of the preceding claims, optionally monoclonal.
7. A DNA sequence comprising either: (a) a sequence set out in Figure 9; (b) any one of the subsequences A to N of Figure 9; (c) the sequence represented by bases 816 to 3204 of Figure 9; (d) a sequence set out in Figure 16; or (e) a DNA sequence hybridizable to (a), (b), (c) or (d); which sequence (a), (b), (c), (d) or (e) encodes a polypeptide which has PI3-kinase activity if expressed in insect cells or is capable of complexing with a p85 mammalian PI3-kinase subunit to produce such activity.
8. A DNA construct comprising a DNA sequence as defined in claim 7 under the control of a control sequence and in proper

reading frame in an expression vector, optionally the control sequence including a regulatable promoter.

5 9. Host cells which have been genetically altered by the incorporation therein of a construct as defined in claim 8, so as to permit expression of the encoded polypeptide, which host cells are optionally insect cells.

10 10. A method for the preparation of a polypeptide encoded by a DNA sequence as defined in claim 7, comprising cultivating host cells as defined in claim 9, which host cells are optionally insect cells.

15 11. A polypeptide obtainable by a method as defined in claim 10, *a*

20 12. The use of a polypeptide as defined in any one of claims 1 to 5 or 11 to provide PI3-kinase activity, either directly or after complexing with a mammalian p85 subunit.

25 13. An enzymatically active complex of a peptide as defined in any one of claims 1 to 5 or 11 and a mammalian p85 subunit.

30 14. A method of prophylaxis or therapy which involves the encouragement or discouragement of cell proliferation by the action of an agonist or antagonist, respectively, for the PI3-kinase activity of a polypeptide as defined in any one of claims 1 to 5 or 11 or of an active complex including the same, wherein said cell proliferation is mediated through a cell surface receptor interactive with said activity.

35 15. A process for obtaining an agonist or antagonist for the PI3-kinase activity of a polypeptide as defined in any one of claims 1 to 5 or 11 or an active complex including the same, which process comprises screening candidate molecules for such activity using a polypeptide as defined in any one of claims 1 to 5 or 11.

16. A process for identifying molecules which bind specifically to a polypeptide as defined in any one of claims 1 to 5 or 11, which process comprises using such a polypeptide in a screening method for such binding.

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17. A pharmaceutical or veterinary formulation comprising an agonist or antagonist for the PI3-kinase activity of a polypeptide as defined in any one of claims 1 to 5 or 11, or an active complex including the same, formulated for
10 pharmaceutical or veterinary use, respectively, optionally together with an acceptable diluent, carrier or excipient and/or in unit dosage form.

18. The use of a polypeptide as defined in any one of claims 1 to 5 or 11, or of an active complex containing said polypeptide, or of an agonist or antagonist thereof, in
15 affecting the level of stimulation of platelets or neutrophils or in regulating blood glucose levels.

19. A method of prophylaxis or therapy including the employment of a polypeptide as defined in any one of claims 1 to 5 or 11, or of an active complex containing said polypeptide, or an agonist or antagonist thereof, in affecting
20 the level of stimulation of platelets or neutrophils or in regulating blood glucose levels.

20. The use of a polypeptide as defined in any of claims 1 to 5 or 11, or of an active complex containing said polypeptide, or of an agonist or antagonist thereof, in the
25 manufacture of a medicament.

21. The use of a polypeptide as defined in any one of claims 1 to 5 or 11, or of an active complex containing said polypeptide, in the in vitro enzymatic production of 3-phosphorylated phosphoinositides.
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22. A phosphorylated phosphoinositide obtained by the performance of the use as defined in claim 21.

23. A phosphotyrosine polypeptide incorporating tyrosine 751 of the human PDGF- β receptor having the capability of binding bovine brain PI3-kinase.

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24. A human PI3-kinase p110 subunit sequence comprising amino acids 19 to 110 of human p110, or an amino terminal truncated or carboxy terminal truncated derivative thereof having less than 20 amino acids deleted from the amino terminal or carboxy terminal end, respectively, but which is capable of binding to a PI3-kinase p85 subunit.

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25. A method of inhibiting p85 and p110 mammalian PI3-kinase subunit interaction, which comprises utilizing a molecule which blocks the binding domain located between amino acids 19 and 110 of human p110.

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26. The use of a sequence or derivative as defined in claim 24 in screening for a therapeutic or prophylactic agent which operates by inhibiting interaction between p85 and p110 mammalian PI3-kinase subunits.

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